## **CLAIMS**

1. A compound of formula (1), or a pharmaceutically acceptable salt, solvate or in vivo by hydrolysable ester thereof:

$$NR^2R^3$$
 $NR^2R^3$ 
 $NR^3$ 
 $NR^2R^3$ 
 $NR^3$ 
 $NR^3$ 

wherein Y is selected from a bond, -S-, -O-, -NR<sup>5</sup>-, -CF<sub>2</sub>-CH<sub>2</sub>-, -CF<sub>2</sub>CF<sub>2</sub>-, -CONR<sup>5</sup>-, 10 phenyl or heteroaryl.

wherein  $R^1$  is a group selected from  $C_{3-7}$ carbocyclyl,  $C_{1-8}$ alkyl,  $C_{2-6}$ alkenyl and  $C_{2-6}$ alkynyl; wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from fluoro, nitrile,  $-OR^4$ ,  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-COOR^7$ ,  $-NR^8COR^9$ ,  $-SR^{10}$ ,  $-SO_2R^{10}$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ , phenyl or heteroaryl; wherein phenyl and heteroaryl are optionally

substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR<sup>4</sup>, -NR<sup>5</sup>R<sup>6</sup>, -CONR<sup>5</sup>R<sup>6</sup>, -COOR<sup>7</sup>, -NR<sup>8</sup>COR<sup>9</sup>, -SR<sup>10</sup>, -SO<sub>2</sub>R<sup>10</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>6</sup>, -NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, C<sub>1-6</sub>alkyl and trifluoromethyl;

wherein R<sup>2</sup> is C<sub>3-7</sub>carbocyclyl, optionally substituted by 1, 2 or 3 substituents independently selected from fluoro, -OR<sup>4</sup>, -NR<sup>5</sup>R<sup>6</sup> -CONR<sup>5</sup>R<sup>6</sup>, -COOR<sup>7</sup>, -NR<sup>8</sup>COR<sup>9</sup>, -SR<sup>10</sup>, -SO<sub>2</sub>R<sup>10</sup>,

20  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ ;

or  $R^2$  is a 3-8 membered ring optionally containing 1, 2 or 3 atoms selected from O, S, -NR<sup>8</sup> and whereby the ring is optionally substituted by  $C_{1-3}$  alkyl or fluoro;

or R<sup>2</sup> is a phenyl or heteroaryl, each of which is optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR<sup>4</sup>, -NR<sup>5</sup>R<sup>6</sup>, -CONR<sup>5</sup>R<sup>6</sup>, -

NR<sup>8</sup>COR<sup>9</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>6</sup>, -NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, C<sub>1-6</sub>alkyl and trifluoromethyl; or R<sup>2</sup> is a group selected from C<sub>1-8</sub>alkyl, C<sub>2-6</sub>alkenyl or C<sub>2-6</sub>alkynyl wherein the group is substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkylamino, di(C<sub>1-6</sub>alkyl)amino, N-(C<sub>1-6</sub>alkyl)-N -(phenyl)amino, N-C<sub>1-6</sub>alkylcarbamoyl,

N,N-di(C<sub>1-6</sub>alkyl)carbamoyl, N-(C<sub>1-6</sub>alkyl)-N-(phenyl)carbamoyl, carboxy, phenoxycarbonyl, -NR<sup>8</sup>COR<sup>9</sup>, -SO<sub>2</sub>R<sup>10</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>6</sup> and -NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>;

wherein R<sup>3</sup> is hydrogen or independently R<sup>2</sup>;

 $R^4$  is hydrogen or a group selected from  $C_{1-6}$ alkyl and phenyl, wherein the group is optionally substituted by 1 or 2 substituents independently selected from halo, phenyl,  $-OR^{11}$  and  $-NR^{12}R^{13}$ ;

R<sup>5</sup> and R<sup>6</sup> are independently hydrogen or a group selected from C<sub>1-6</sub>alkyl and phenyl wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, phenyl, -OR<sup>14</sup>,-NR<sup>15</sup>R<sup>16</sup>, -COOR<sup>14</sup>, -CONR<sup>15</sup>R<sup>16</sup>, -NR<sup>15</sup>COR<sup>16</sup>, -SO<sub>2</sub>R<sup>10</sup>, -SONR<sup>15</sup>R<sup>16</sup> and NR<sup>15</sup>SO<sub>2</sub>R<sup>16</sup>

or

R<sup>5</sup> and R<sup>6</sup> together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring is optionally substituted by 1, 2 or 3

- substituents independently selected from phenyl,  $-OR^{14}$ ,  $-COOR^{14}$ ,  $-NR^{15}R^{16}$ ,  $-CONR^{15}R^{16}$ ,  $-NR^{15}COR^{16}$ ,  $-SO_2R^{10}$ ,  $-SONR^{15}R^{16}$ ,  $NR^{15}SO_2R^{16}$  or  $C_{1}$ -alkyl (optionally substituted by 1 or 2 substituents independently selected from halo,  $-NR^{15}R^{16}$  and  $-OR^{17}$  groups);  $R^{10}$  is hydrogen or a group selected from  $C_{1}$ -alkyl or phenyl, wherein the group is optionally
- substituted by 1, 2 or 3 substituents independently selected from halo, phenyl, -OR<sup>17</sup> and 20 NR<sup>15</sup>R<sup>16</sup>; and each of R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>11</sup>, R<sup>12</sup>, R<sup>13</sup>, R<sup>14</sup> R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup> is independently hydrogen,
  C<sub>1-6</sub>alkyl or phenyl;
  - R<sup>x</sup> is trifluoromethyl, -NR<sup>5</sup>R<sup>6</sup>, phenyl, napthyl, monocyclic or bicyclic heteroaryl wherein a heteroring may be partially or fully saturated and one or more ring carbon atoms may form a carbonyl group, and wherein each phenyl or heteroaryl group is optionally substituted by 1, 2
- or 3 substituents independently selected from halo, cyano, nitro, -OR<sup>4</sup>, -NR<sup>5</sup>R<sup>6</sup>, -CONR<sup>5</sup>R<sup>6</sup>, -COR<sup>7</sup>, -COOR<sup>7</sup>, -NR<sup>8</sup>COR<sup>9</sup>, -SR<sup>10</sup>, -SO<sub>2</sub>R<sup>10</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>6</sup>, -NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, C<sub>1-6</sub>alkyl or trifluoromethyl;;
  - or  $R^x$  is a group selected from  $C_{3-7}$  carbocyclyl,  $C_{1-8}$  alkyl,  $C_{2-6}$  alkenyl and  $C_{2-6}$  alkynyl whereby the group is optionally substituted by 1, 2 or 3 substituents independently selected from halo,
- -OR<sup>4</sup>, -NR<sup>5</sup>R<sup>6</sup>, -CONR<sup>5</sup>R<sup>6</sup>, -COR<sup>7</sup>, -COOR<sup>7</sup>, -NR<sup>8</sup>COR<sup>9</sup>, -SR<sup>10</sup>, -SO<sub>2</sub>R<sup>10</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>6</sup>, -NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, phenyl or heteroaryl; and wherein each phenyl or heteroaryl group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR<sup>4</sup>, -

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 $NR^5R^6$ ,  $-CONR^5R^6$ ,  $-COR^7$ ,  $-COOR^7$ ,  $-NR^8COR^9$ ,  $-SR^{10}$ ,  $-SO_2R^{10}$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ ,  $C_{1-6}$ alkyl or trifluoromethyl;

- 2. A compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof according to claim 1 wherein R<sup>2</sup> is C<sub>1-8</sub>alkyl optionally substituted by 1 or 2 hydroxy substituents.
- 3. A compound, pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof according to claim 1 wherein R<sup>1</sup> is benzyl or -CH<sub>2</sub>CH<sub>2</sub>OPh, or CH<sub>2</sub>CH<sub>2</sub>Ph wherein in each case the phenyl ring is optionally substituted by 1, 2 or 3 substituents independently selected from fluoro, chloro, bromo, methoxy, methyl and trifluoromethyl.
  - 4. A compound, pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof wherein R<sup>3</sup> is hydrogen.
  - 5. A compound, pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof wherein Y is selected from a bond, -S-, and -CF<sub>2</sub>-CH<sub>2</sub>- and -CH<sub>2</sub>-CH<sub>2</sub>-.
- 6. A compound, pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof wherein R<sup>x</sup> is methyl,1-methylimidazolyl, 1,2-dimethylimidazolyl, N,N-dimethylamino, azetidinyl, pyrolidinyl, morpholinyl, piperidinyl and trifluoromethyl
  - 7. A compound selected from the group consisting of:

N-[4-[[(2,3-difluorophenyl)methyl]thio]-6-[[(1R)-2-hydroxy-1-methylethyl]amino]-1,3,5-

25 triazin-2-yl]-methanesulfonamide; and

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N-[4-[[(2,3-difluorophenyl)methyl]thio]-6-[[(1R)-2-hydroxy-1-methylethyl]amino]-1,3,5-triazin-2-yl]-1-azetidinesulfonamide, N-[4-[[(2,3-difluorophenyl)methyl]thio]-6-[[(1R)-2-

hydroxy-1-methylethyl]amino]-1,3,5-triazin-2-yl]-methanesulfonamide

- N-[4-[[(2,3-difluorophenyl)methyl]thio]-6-[[(1R)-2-hydroxy-1-methylethyl]amino]-1,3,5-
- 30 triazin-2-yl]-1-azetidinesulfonamide

4-morpholinesulfonamide, N-[4-[[(2,3-difluorophenyl)methyl]thio]-6-[[(1R)-2-hydroxy-1-methylethyl]amino]-1,3,5-triazin-2-yl]-

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methanesulfonamide, N-[4-[[2-(2,3-difluorophenoxy)ethyl]thio]-6-[[(1R)-2-hydroxy-1-methylethyl]amino]-1,3,5-triazin-2-yl]-

- methanesulfonamide, 1,1,1-trifluoro-*N*-[4-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-6-(2-phenylethyl)-1,3,5-triazin-2-yl]- or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof.
  - 8. A compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof according to any one of claims 1 to 7 for use as a medicament.
- 9. A compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof according to any one of claims 1 to 7 for use as a medicament for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis..
- 15 10. A compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof according to any one of claims 1-7, for use as a medicament for the treatment of cancer.
- 11. The use of a compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, according to any one of claims 1 to 7 in the manufacture of a medicament for the treatment of human diseases or conditions in which modulation of chemokine receptor activity is beneficial.
- 12. The use of a compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, according to any one of claims 1 to 7 in the manufacture of a medicament for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, irritable bowel syndrome, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.
- 30 13. The use of a compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, according to any one of claims 1 to 7 in the manufacture of a medicament for the treatment of cancer.

- 14. A pharmaceutical composition comprising a compound, or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof according to any one of claims 1 to 7; and a pharmaceutically-acceptable diluent or carrier.
- 5 15. A process for the preparation of a compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, which comprises the steps of: treating a compound of formula (2):

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wherein Y, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are as defined in formula (1) with a sulfonamide of formula R<sup>x</sup>SO<sub>2</sub>NH<sub>2</sub> where R<sup>x</sup> is as defined in formula (1);

- 15 and optionally thereafter, one or more of steps (i), (ii), (iii), (iv), or (v) in any order:
  - i) removing any protecting groups;
  - ii) converting the compound of formula (1) into a further compound of formula (1)
  - iii) forming a salt
  - iv) forming a prodrug
- 20 v) forming an in vivo hydrolysable ester.
- 16. A combination therapy which comprises administering a compound of formula (1) or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, or a pharmaceutical composition or formulation comprising a compound of formula (1),
  25 concurrently or sequentially with other therapy and/or another pharmaceutical agent.
  - 17. A combination therapy as claimed in claim 16 for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, irritable bowel syndrome, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

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- 18. A combination therapy as claimed in claim 16 for the treatment of cancer.
- 19. A pharmaceutical composition which comprises a compound of formula (1) or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, in conjunction
  5 with another pharmaceutical agent.
  - 20. A pharmaceutical compositon as claimed in claim 19 for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, irritable bowel syndrome, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

21. A pharmaceutical composition as claimed in claim 19 for the treatment of cancer.

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